ISSN 1070-4280, Russian Journal of Organic Chemistry, 2006, Vol. 42, No. 10, pp. 1528–1531. © Pleiades Publishing, Inc., 2006.
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Oxidative Dehydrobromination of 3-(α-Bromobenzyl)quinoxalin-2(1*H*)-ones according to Kornblum as a Simple and Efficient Synthetic Route to Quinoxalyl Aryl Ketones

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Received July 21, 2005

Abstract—Condensation of ethyl 3-aryl-3-bromo-2-oxopropanoates with *o*-phenylenediamine in acetic acid gave 3-(α-bromobenzyl)quinoxalin-2(1*H*)-ones which were converted in high yield into the corresponding 3-aroylquinoxalin-2(1*H*)-ones via oxidative dehydrobromination in dimethyl sulfoxide according to Kornblum.

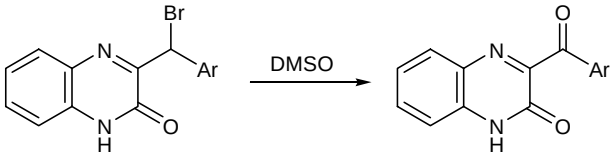
DOI: 10.1134/S107042800610023X

3-Benzoylquinoxalin-2(1*H*)-one contains β-dicarbonyl and α-iminocarbonyl fragments in combination with other functional groups, which makes it the key compound in the synthesis of various polycyclic systems via fusion at the *a* and *b* sides of the quinoxaline ring [1–10]. Preparative accessibility of this compound and its derivatives substituted at the benzoyl fragment could open new prospects in the synthesis of various fused heterocyclic systems.

In continuation of our studies [11–13] on the synthesis and application of 3-benzoylquinoxalin-2(1*H*)-one, the present communication describes a convenient and efficient one-step procedure for the preparation of both 3-benzoylquinoxalin-2(1*H*)-one and its derivatives substituted at the benzene ring.

We previously showed [12] that standard conditions for the Kornblum oxidation (heating of an organic halogen compound or its analog in DMSO in the presence of sodium acetate or urea [14, 15]) ensure preparation of 3-benzoylquinoxalin-2(1*H*)-one from 3-(α-chlorobenzyl)quinoxalin-2(1*H*)-one in 84% yield. In the absence of sodium acetate, the yield does not exceed 30%, regardless of the reactant ratio and reaction time. We found that the use in this reaction of the corresponding bromo derivatives instead of chloride makes it possible to avoid synthesis of thiocyanato or azido derivatives; moreover, in this case there is no need of using sodium acetate as deprotonating agent. Presumably, the role of the latter is played by quinoxalines themselves. Keeping of compounds **Ia**–**Ie** in dimethyl sulfoxide for a short time is sufficient to obtain the corresponding ketones **IIa**–**IIe** in high yield (Scheme 1).

Scheme 1.

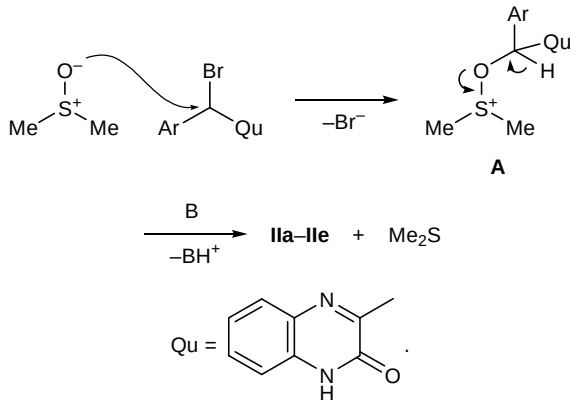


Ia–Ie **IIa–IIe**

Ar = Ph (**a**), 4-BrC_6H_4 (**b**), 2,4-$Cl_2C_6H_3$ (**c**), 3-$O_2NC_6H_4$ (**d**), 4-$O_2NC_6H_4$ (**e**).

The mechanism of formation of hetaryl ketones **IIa**–**IIe** is likely to include replacement of the bromine atom in **Ia**–**Ie** by dimethyl sulfoxide with formation of

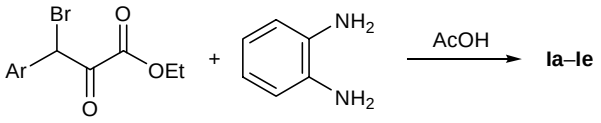
Scheme 2.



alkoxysulfonium salt **A** which undergoes deprotonation by the action of the initial quinoxaline or DMSO in the second step. As a result, the corresponding aryl quinoxalyl ketone and dimethyl sulfide (departing group) [16] are formed (Scheme 2).

Initial 3-(α-bromobenzyl)quinoxalin-2(1*H*)-ones **Ia**–**Ie** were synthesized in quantitative yield by reaction of ethyl 3-aryl-3-bromo-2-oxopropanoates **IIIa**–**IIIe** with *o*-phenylenediamine in acetic acid [17] (Scheme 3).

Scheme 3.



IIIa–IIIe

Ar = Ph (**a**), 4-BrC_6H_4 (**b**), 2,4-$Cl_2C_6H_3$ (**c**), 3-$O_2NC_6H_4$ (**d**), 4-$O_2NC_6H_4$ (**e**).

The structure of compounds **Ia**–**Ie** and **IIa**–**IIe** was confirmed by the analytical and spectral (IR and ^{1}H NMR) data; quinoxalinone **IIa** was also identified by comparison with an authentic sample. The IR spectra of **IIa**–**IIe** lacked absorption at 576±20 cm^{-1}, typical of stretching vibrations of the C–Br bond in initial compounds **Ia**–**Ie**; the bands belonging to the lactam carbonyl group (1665±5 cm^{-1}) and C=N bond (1608±3 cm^{-1}) were displaced to lower frequencies, and a new carbonyl absorption band appeared at 1698±10 cm^{-1} due to ketone group. The ^{1}H NMR spectra of **IIa**–**IIe** contained no benzylic proton signal (δ 6.52±0.43 ppm). These data indicated formation of 3-aroylquinoxalin-2(1*H*)-ones as a result of oxidative dehydrobromination of 3-(α-bromobenzyl) derivatives.

EXPERIMENTAL

The IR spectra were recorded on a Bruker Vector-22 spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were obtained from solutions in DMSO-d_6 on a Bruker MSL-400 spectrometer (400.13 MHz); the chemical shifts were measured relative to the signal from residual protons in the solvent. The melting points were determined on a Boetius melting point apparatus.

3-(α-Bromobenzyl)quinoxalin-2(1*H*)-one (Ia). *o*-Phenylenediamine, 0.4 g (4 mmol), was added under stirring (magnetic stirrer) to a solution of 1.08 g (4 mmol) of bromopyruvate **IIIa** in acetic acid. The mixture slightly warmed up (by 5–10°C), *o*-phenylenediamine quickly dissolved, and abundant solid precipitated almost instantaneously (within 3–5 min). The mixture was stirred for an additional 1.5 h, and the precipitate was filtered off and washed with isopropyl alcohol (2×15 ml). Yield 0.97 g; an additional amount of the product, 0.15 g, separated from the filtrate on storage. Overall yield 1.12 g (89%), mp 194–197°C. IR spectrum, ν, cm^{-1}: 556, 596, 692, 758, 915, 1497, 1556, 1610, 1666, 2716, 3058, 3094. ^{1}H NMR spectrum δ, ppm: 6.79 s (1H), 7.83 d.d (2H, 7-H, *m*-H, *J* = 10.56, 7.52 Hz), 7.73 d (2H, 5-H, *o*-H, *J* = 7.52 Hz), 7.63–7.27 m (5H), 12.57 s (1H, NH). Found, %: C 57.51; H 3.41; Br 21.92; N 8.82. $C_{15}H_{11}BrN_2O$. Calculated, %: C 57.16; H 3.52; Br 25.35; N 8.89.

Compounds **Ib**–**Ie** were synthesized following a similar procedure.

3-(α,4-Dibromobenzyl)quinoxalin-2(1*H*)-one (Ib). Yield 91%, mp 257–259°C. IR spectrum, ν, cm^{-1}: 474, 575, 762, 848, 911, 1011, 1489, 1555, 1595, 1611, 1667, 2720, 3098, 3161. ^{1}H NMR spectrum, δ, ppm: 6.77 s (1H), 7.34–7.49 m (2H), 7.58–7.70 m (5H), 7.80 d (1H, 5-H, *J* = 8.00 Hz), 12.67 s (1H, NH). Found, %: C 46.37; H 2.48; Br 41.05; N 6.81. $C_{15}H_{10}Br_2N_2O$. Calculated, %: C 45.72; H 2.56; Br 40.55; N 7.11.

3-(α-Bromo-2,4-dichlorobenzyl)quinoxalin-2(1*H*)-one (Ic). Yield 58%, mp 231–233°C. IR spectrum, ν, cm^{-1}: 431, 466, 582, 610, 747, 763, 858, 908, 1049, 1101, 1148, 1433, 1499, 1558, 1588, 1612, 1660, 3011, 3100, 3164, 3310. ^{1}H NMR spectrum, δ, ppm: 7.04 s (1H), 7.36 d.d (1H, 7-H, *J* = 7.24, 8.40 Hz), 7.40 d (1H, 8-H, *J* = 8.40 Hz), 7.54 d (1H, 5'-H, *J* = 8.40 Hz), 7.62 d.d (1H, 6-H, *J* = 7.60, 7.24 Hz), 7.69 s (1H, 3'-H), 7.79 d (1H, 5-H, *J* = 7.60 Hz), 7.92 d (1H, 6'-H, *J* = 8.40 Hz), 12.73 s (1H, NH). Found, %: C 47.67; H 2.15; Br 20.71; Cl 18.41; N 7.02. $C_{15}H_9BrCl_2N_2O$. Calculated, %: C 46.91; H 2.36; Br 20.80; Cl 18.46; N 7.29.

3-(α-Bromo-3-nitrobenzyl)quinoxalin-2(1*H*)-one (Id). Yield 69%, mp 244–247°C. IR spectrum, ν, cm^{-1}: 413, 597, 697, 765, 814, 910, 931, 1076, 1154, 1292, 1353, 1502, 1525, 1541, 1670, 2721. ^{1}H NMR spectrum, δ, ppm: 6.95 s (1H), 7.36 d (1H, 8-H, *J* = 7.60 Hz), 7.38 d.d (1H, 6-H, *J* = 7.60, 7.60 Hz), 7.62 d.d (1H, 7-H, *J* = 7.60, 7.60 Hz), 7.74 d.d (1H, 5'-H, *J* = 8.60, 7.96 Hz), 7.78 d (1H, 6'-H, *J* = 8.60 Hz), 8.19 d (1H, 5-H, *J* = 7.60 Hz), 8.25 d (1H, 4'-H, *J* = 7.96 Hz), 8.64 s (1H, 2'-H), 12.76 s (1H,

NH). Found, %: C 49.61; H 2.27; Br 21.18; N 11.14. $C_{15}H_{10}BrN_3O_3$. Calculated, %: C 50.02; H 2.80; Br 22.19; N 11.07.

3-(α-Bromo-4-nitrobenzyl)quinoxalin-2(1*H*)-one (Ie). Yield 65%, mp 270–273°C. IR spectrum, ν, cm^{-1}: 413, 579, 757, 766, 851, 869, 911, 1111, 1294, 1320, 1351, 1437, 1491, 1514, 1603, 1668, 2720, 3476. ^1H NMR spectrum, δ, ppm: 6.86 s (1H), 7.35 d.d (1H, 6-H, *J* = 8.24, 8.92 Hz), 7.36 d (1H, 8-H, *J* = 7.44 Hz), 7.57 d.d (1H, 7-H, *J* = 7.44, 8.24 Hz), 7.76 d (2H, 2'-H, 6'-H, *J* = 8.24 Hz), 7.97 d (2H, 3'-H, 5'-H, *J* = 8.24 Hz), 7.98 d (1H, 5-H, *J* = 8.92 Hz), 12.46 s (1H, NH). Found, %: C 49.61; H 2.47; Br 22.10; N 11.14. $C_{15}H_{10}BrN_3O_3$. Calculated, %: C 50.02; H 2.80; Br 22.19; N 11.07.

3-Aroylquinoxalin-2(1*H*)-ones IIa–IIe (*general procedure*). A solution of 2 mmol of 3-(α-bromobenzyl)quinoxalin-2(1*H*)-one **Ia**–**Ie** in 10 ml of DMSO was kept for 10–15 min and poured into 25 ml of water, and the precipitate was filtered off and washed with water (2×15 ml).

3-Benzoylquinoxalin-2(1*H*)-one (IIa). Yield 96%. Its properties and spectral parameters were in agreement with those reported in [18].

3-(4-Bromobenzoyl)quinoxalin-2(1*H*)-one (IIb). Yield quantitative, mp 280–282°C (from AcOH). IR spectrum, ν, cm^{-1}: 566, 757, 842, 897, 917, 1068, 1151, 1253, 1293, 1304, 1395, 1495, 1569, 1590, 1606, 1652, 1700, 3096, 3568. ^1H NMR spectrum, δ, ppm: 7.40 d.d (1H, 7-H, *J* = 7.52, 7.52 Hz), 7.48 d (1H, 8-H, *J* = 7.52 Hz), 7.68 d.d (1H, 6-H, *J* = 7.52, 8.24 Hz), 7.80 d (2H, 3'-H, 5'-H, *J* = 8.24 Hz), 7.85 d (1H, 5-H, *J* = 8.24 Hz), 7.93 d (2H, 2'-H, 6'-H, *J* = 8.24 Hz), 8.32 br.s (1H, NH). Found, %: C 57.50; H 2.60; Br 24.54; N 8.88. $C_{15}H_9BrN_2O_2$. Calculated, %: C 54.74; H 2.76; Br 24.28; N 8.51.

3-(2,4-Dichlorobenzoyl)quinoxalin-2(1*H*)-one (IIc). Yield quantitative, mp 240–242°C (from AcOH). IR spectrum, ν, cm^{-1}: 425, 600, 774, 806, 830, 855, 923, 958, 1057, 1102, 1162, 1260, 1297, 1422, 1495, 1553, 1582, 1611, 1663, 1688, 3069, 3215, 3567. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 7.36 d.d (1H, 6-H, *J* = 7.52, 6.84 Hz), 7.40 d (1H, 8-H, *J* = 8.24 Hz), 7.61 d.d (1H, 3'-H, *J* = 8.24, *J* 2.04 Hz), 7.66 d.d (1H, 7-H, *J* = 6.84, 8.24 Hz), 7.75 d (1H, 5'-H, *J* = 2.04 Hz), 7.79 d (1H, 5-H, *J* = 7.52 Hz), 7.88 d (1H, 6'-H, *J* = 8.24 Hz), 8.26 s (1H, NH). Found, %: C 57.35; H 2.37; Cl 20.44; N 8.79. $C_{15}H_8Cl_2N_2O_2$. Calculated, %: C 56.45; H 2.53; Cl 22.22; N 8.78.

3-(3-Nitrobenzoyl)quinoxalin-2(1*H*)-one (IId). Yield quantitative, mp 285–287°C (from AcOH). IR spectrum, ν, cm^{-1}: 418, 571, 695, 755, 875, 897, 936, 1095, 1219, 1251, 1305, 1320, 1352, 1497, 1529, 1611, 1654, 1708, 3088. ^1H NMR spectrum, δ, ppm: 7.42 d.d (1H, 6-H, *J* = 7.52, 6.88 Hz), 7.47 d (1H, 8-H, *J* = 7.56 Hz), 7.71 d.d (1H, 7-H, *J* = 7.56, 7.52 Hz), 7.87 d (1H, 5'-H, *J* = 8.20 Hz), 7.91 d.d (1H, 6'-H, *J* = 7.56, 8.24 Hz), 8.44 d (1H, 4'-H, *J* = 7.56 Hz), 8.56 d (1H, 5-H, *J* = 6.84 Hz), 8.74 s (1H, 2'-H), 12.81 s (1H, NH). Found, %: C 62.55; H 4.09; N 13.61. $C_{15}H_9N_3O_4$. Calculated, %: C 61.02; H 3.07; N 14.23.

3-(4-Nitrobenzoyl)quinoxalin-2(1*H*)-one (IIe). Yield quantitative, mp 302–304°C (from AcOH). IR spectrum, ν, cm^{-1}: 569, 698, 754, 851, 866, 919, 1026, 1150, 1253, 1294, 1351, 1515, 1606, 1655, 1703, 2954, 3433. ^1H NMR spectrum, δ, ppm: 7.38 d.d (1H, 6-H, *J* = 8.24, 6.88 Hz), 7.45 d (1H, 8-H, *J* = 7.60 Hz), 7.67 d.d (1H, 7-H, *J* = 6.88, 7.60 Hz), 7.82 d (1H, 5-H, *J* = 8.24 Hz), 8.22 d (2H, 2'-H, 6'-H, *J* = 8.88 Hz), 8.34 d (1H, 3'-H, 5'-H, *J* = 8.88 Hz), 12.81 s (1H, NH). Found, %: C 60.73; H 3.01; N 14.32. $C_{15}H_9N_3O_4$. Calculated, %: C 61.02; H 3.07; N 14.23.

REFERENCES

1. Zimmer, H., Amer, A., Ho, D., and Palmer-Sungail, R., *J. Heterocycl. Chem*., 1991, vol. 28, p. 1501.
2. Markees, D.G., *J. Heterocycl. Chem*., 1989, vol. 26, p. 29.
3. Matoba, K., Iton, K., Kondo, K., Yamazaki, T., and Nagata, M., *Chem. Pharm. Bull*., 1981, vol. 29, p. 2442.
4. Matoba, K., Iton, K., Nagata, M., and Yamazaki, T., *Heterocycles*, 1980, vol. 14, p. 465.
5. Matoba, K., Terada, T., Suguira, M., and Yamazaki, T., *Heterocycles*, 1987, vol. 26, p. 55.
6. Matoba, K., Miyata, Y., and Yamazaki, T., *Chem. Pharm. Bull*., 1983, vol. 31, p. 476.
7. Atfah, A., Abu-Shuheil, M.Y., and Hill, J., *Tetrahedron Lett*., 1990, vol. 46, p. 6483.
8. Eiden, F. and Bachmann, G., *Arch. Pharm*., 1973, vol. 306, p. 876.
9. Glushkov, R.G., Dronova, L.N., Elina, A.S., Musatova, I.S., Porokhovaya, M.V., Solov'eva, N.P., Chistyakov, V.V., and Sheinker, Yu.N., *Khim.-Farm. Zh*., 1988, no. 3, p. 336.
10. Kurasawa, Y., Ichikawa, M., and Takada, A., *Heterocycles*, 1988, vol. 20, p. 269.
11. Mamedov, V.A., Kalinin, A.A., Rizvanov, I.Kh., Azancheev, N.M., Efremov, Yu.Ya., and Levin, Ya.A., *Khim. Geterotsikl. Soedin*., 2002, no. 9, p. 1279.

12. Mamedov, V.A., Kalinin, A.A., Gubaidullin, A.T., Litvinov, I.A., and Levin, Ya.A., *Khim. Geterotsikl. Soedin*., 2002, no. 12, p. 1704.
13. Mamedov, V.A., Kalinin, A.A., Gubaidullin, A.T., Rizvanov, I.Kh., Chernova, A.V., Doroshkina, G.M., Litvinov, I.A., and Levin, Ya.A., *Russ. J. Org. Chem*., 2003, vol. 39, p. 131.
14. Kornblum, N., Jones, W.J., and Anderson, G.J., *J. Am. Chem. Soc*., 1959, vol. 81, p. 4113.
15. Kornblum, N. and Frazier, H.W., *J. Am. Chem. Soc*., 1966, vol. 88, p. 865.
16. Smith, M.B. and March, J., *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, New York: Wiley, 2001, 5th ed., p. 1535.
17. Mamedov, V.A., Mustakimova, L.V., Gorbunova, E.A., and Levin, Ya.A., *Novye dostizheniya v khimii karbonil'nykh i geterotsiklicheskikh soedinenii* (Advances in the Chemistry of Carbonyl and Heterocyclic Compounds), Saratov, 2000, p. 150.
18. Mamedov, V.A., Kalinin, A.A., Gubaidullin, A.T., Litvinov, I.A., and Levin, Ya.A., *Khim. Geterotsikl. Soedin*., 2003, p. 101.